

REMARKS

THE CLAIM AMENDMENTS:

Claim 1 has been amended to more fully define the invention. Support for the amendment to claim 1 is found in the specification at, *inter alia*, page 7, lines 7-11.

With this amendment, claims 2-5, 25, and 26 have been canceled.

The amendments to claims 21 and 38 are discussed below under the subheadings relating to the Examiner's claim objections and indefiniteness rejections.

Claim 28 has been rewritten to more clearly define the subject matter described therein. The rewriting of the claim language adds no new matter to the application.

Claim 33 has been amended to depend from claim 30 rather than claim 7 in order to provide an antecedent basis for the term "the signature sequence" in claim 33.

In addition, to more fully define the invention, new claims 115 to 118 have been added to the application. Support for the recitation of the degenerately pairing nucleotide analogs of claims 115 and 116 is found in the specification at, *inter alia*, the Brief Description of the Figures at page 9, lines 22-29; Figures 1A, 1B, 2, and 3; page 15, lines 28-29; page 21, line 18 to page 23, line 9; page 24, line 10 to page 25, line 6; and page 43, lines 3-9. Support for the recitation of the variable nucleotides of claims 117 to 118 is found in the specification at, *inter alia*, page 14, line 25; page 20, lines 4-5; and page 24, line 10 to page 26, line 9.

No new matter has been added to the application with any of the claim amendments made in this paper.

THE CLAIM OBJECTIONS:

The Examiner has objected to claims 6 and 22 on the grounds that the phrase "used for" should be "is used for." Applicants respectfully traverse this objection on the grounds that the phrase "used for" is correct and represents proper claim language. Specifically, as it stands, claim 6 reads: "The method of claim 1 used for sequencing the target nucleic acid analyte." Applicants submit that this is a fully comprehensible and understandable sentence that comports to well-established claim language principles. Similarly, claim 22 is also a complete sentence that represents well-established claim language; as it stands, claim 22 reads: "The method of claim 1 used for allelic analysis." By contrast, the Examiner proposes the following language for claims 6 and 22, respectively: "The method of claim 1 is used for sequencing the target nucleic acid analyte" and "The method of claim 1 is used for allelic analysis." Applicants submit that this language proposed by the Examiner is *not* in the form that is well-established

and generally accepted for claim language. Accordingly, applicants respectfully request that the Examiner reverse the objections to claims 6 and 22 and accept these claims as they presently stand. If the Examiner maintains this objection, applicants respectfully request that the Examiner provide proof that the Office finds applicants' claim language objectionable and that the Office finds the Examiner's proposed claim language to be the preferred language for dependent claims.

The Examiner has also objected to claim 38 as in improper dependent form. Applicants have amended claim 38 to depend from claim 29; the reference to claim 39 was a typographical error from a previous amendment. Applicants thank the Examiner for noticing the discrepancy in claim language.

THE CLAIM REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH:

Claims 1, 2, 5-15, 18-25, 27-31, and 36-39 stand rejected as indefinite under 35 U.S.C. § 112, second paragraph. Each of the Examiner's rejections are addressed in numerical order by item number.

Item 8. Claim 1 has been rewritten so that it no longer includes the allegedly indefinite language identified by the Examiner. Accordingly, applicants respectfully request reconsideration and withdrawal of this rejection.

Item 9. Applicants respectfully traverse the Examiner's rejection of the "contacting" step of claim 1 as indefinite for the following reasons.

The Examiner states that because "the position of interest in each oligonucleotide is not complementary to the target sequence...there is a mismatch at the position of interest in each oligonucleotide...[t]herefore, the hybridization of the analyte and [the] at least two oligonucleotide probes cannot occur in the claim." The Examiner's statement demonstrates a misunderstanding of the invention. As a preliminary matter, applicants note that the position of interest is not on the oligonucleotide probe; rather, it is in the target sequence segment of the target nucleic acid analyte. Secondly, because the oligonucleotide probe is designed to have a variable position, hybridization will occur where there is complementarity between the nucleotide at the variable position of the oligonucleotide probes and a nucleotide at a corresponding position on the target sequence segment. Claim 1 has been amended to more fully define this unique and novel feature of the invention. Because claim 1 is clear on the method by which the variable position of the oligonucleotide probes may be used to hybridize with a corresponding nucleotide on the target sequence segment of the target nucleic acid analyte, applicants respectfully request reconsideration and withdrawal of this rejection.

Item 10. With the cancellation of claim 5, this rejection is rendered moot.

Item 11. The Examiner's rejection of claims 6, 10, 14, and 22 is rendered moot for cancelled claim 6 and is respectfully traversed for claims 10, 14, and 22 for the reasons set forth above in the

discussion of claim 1. Accordingly, applicants respectfully request reconsideration and withdrawal of this rejection.

Item 12. The Examiner's rejection of claims 18 and 21 is also traversed for the reasons set forth in the discussion of claim 1. With respect to the Examiner's rejection of claim 21 as lacking a verb, the verb "used" has been added to this claim. Applicants thank the Examiner for noticing this omission.

Item 13. In response to the Examiner's rejection of claim 20 as lacking antecedent basis, applicants have added a "the" before the term "hybridized nucleic acids." Applicants thank the Examiner for noticing this omission.

CLAIM REJECTION UNDER 35 U.S.C. § 102

Claims 1, 6, 18, 19, 23, and 24 stand rejected under 35 U.S.C. § 102(e) as anticipated by Senapathy. This rejection is respectfully traversed.

As explained above and as recited in claim 1, the present invention is directed to a method of employing oligonucleotide probes to obtain information on a target nucleic acid analyte containing a target sequence segment, the method comprising contacting the analyte, under hybridizing conditions, with at least two oligonucleotide probes that have at least one overlapping nucleotide in common and at least one variable nucleotide, wherein hybridization of one, some, or all of the at least two oligonucleotide probes to the target sequence segment occurs only if the at least one variable nucleotide of the at least one oligonucleotide probe base pairs with a corresponding nucleotide on the target sequence segment.

An advantage of the claimed method is the reduction in the number of unique hybridizing sequences that are required to hybridize to a nucleic acid sequence of interest (page 6, lines 16-18). Accordingly, the information that is obtained from the method is identification of a variable position of the target nucleic acid analyte that may base pair with a degenerate base. In this way, fewer oligonucleotide probes may be made for the amplification or sequencing of a particular target nucleic acid analyte.

Senapathy teaches a method for sequencing and amplifying nucleic acid templates using a full-length primer with a fixed sequence and a random sequence (col. 3, ll. 7-13). The fixed sequence anchors the primer on the template DNA at its complementary sequence (col. 6, ll. 45-47) and the random sequence provides one full-length primer and many near full-length primer species that bind to complementary flanking sequences (col. 6, ll. 47-50). Because the fixed sequence anchors the primer, primers with mismatches will still bind to the nucleic acid template (col. 6, ll. 39-41).

The primers of Senapathy differ from those of the claimed invention in several respects. First, under the method of Senapathy, information on the nucleotide sequence of interest may be obtained with

one primer; thus, there is no requirement that at least two oligonucleotide primers are required as there is in the claimed invention. Second, the primers of Senapathy are not designed to have at least a one-nucleotide overlap as are those of the claimed invention; rather, the primers of Senapathy are designed based upon the presence of a fixed nucleotide sequence and a series of random sequences. Third, the primers of Senapathy are designed to hybridize in the presence of nucleotidic mismatches at the random sequence, whereas the oligonucleotide probes of the claimed invention will *not* hybridize in the presence of a nucleotidic mismatch at the variable positions of the oligonucleotide primers.

Because Senapathy does not teach or suggest a method for using at least two oligonucleotide probes with at least one nucleotide overlap and at least one variable position to obtain information on a target nucleic acid analyte with a target sequence segment, wherein hybridization does *not* occur where there is a mismatch at the variable position of the oligonucleotide primers, it follows that Senapathy does not anticipate or render the claimed invention obvious. Accordingly, since Senapathy does not anticipate the claimed invention, applicants respectfully request reconsideration and withdrawal of this rejection.

CLAIM REJECTION UNDER 35 U.S.C. § 103

Claims 21 and 22 stand rejected under 35 U.S.C. § 103(a) as obvious over Senapathy in view of Santamaria et al. This rejection is respectfully traversed.

The Examiner cites the secondary reference Santamaria et al. for the teaching of a DNA sequenced-based HLA typing method that may be used for genetic analysis such as allelic analysis.

The hypothetical combination of Senapathy in view of Santamaria et al. is cited against dependent claims 21 and 22, both of which ultimately depend from claim 1.

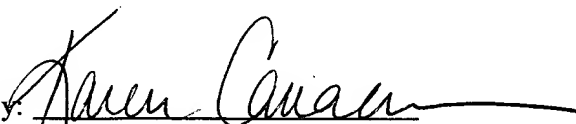
Because the primary reference, Senapathy, does not anticipate or render obvious the claimed invention as recited in claim 1, the additional teachings of Santamaria et al. cannot serve to render the invention of claims 21 and 22 obvious. Accordingly, since the hypothetical combination of Senapathy in view of Santamaria et al. does not render the claimed invention obvious, applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

Because all of the claim objections and claim rejections set forth by the Examiner have been addressed, resolved, and overcome with this Amendment, applicants respectfully request withdrawal of all claim objections and rejections and passage of this application to allowance.

Should the Examiner wish to discuss this Amendment, he is welcome to contact the undersigned attorney at 650-330-4913 or at canaan@reedpatent.com.

Respectfully submitted,

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